

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) *22 OCT 2005* see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No
PCT/US2004/039775

International filing date (day/month/year)
21.12.2004

Priority date (day/month/year)
22.12.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/4196, A61K31/4245, A61K31/433, C07D249/08, C07D271/10, C07D285/12, A61P3/10

Applicant
ELI LILLY AND COMPANY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis 1(a)(i) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/US2004/039775**IP20 Rec'd PCT/PTO 19 MAY 2006****Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/039775

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 57-61,63,65,65

because:

☒ the said international application, or the said claims Nos. 57-61,63,65,65 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/039775

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-84
Inventive step (IS)	Yes: Claims	
	No: Claims	1-84
Industrial applicability (IA)	Yes: Claims	1-56, 62, 64, 67-84
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

PCT/US2004/039775

Re Item III**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The present claim set encompassed so many compounds that it is impossible to cite all documents which are relevant to the issue of novelty. The 9 X-documents cited in the search report have been cited only exemplarily.

The search has therefore been limited to compounds of the present claim 1 wherein V is a C0-8-alkyl, Y is C, O, S or N (i.e. not a single bond) and E is C(R3R4)A.

Claims 57-61, 63, 65 and 65 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

The following documents have been cited in the International Search Report:

- D1: WO 03/084916 A (WARNER-LAMBERT) 16 October 2003 (2003-10-16)
- D2: MEANWELL ET AL: JOURNAL OF MEDICINAL CHEMISTRY, vol. 35, no. 19, 1992, pages 3498-3512, XP002322862
- D3: EP-A-0 453 846 (BAYER) 30 October 1991 (1991-10-30)
- D4: US-A-3 637 672 (OSAKA SEIKA KOGYO) 25 January 1972 (1972-01-25)
- D5: WO 97/03967 A (RHONE-POULENC RORER) 6 February 1997 (1997-02-06)
- D6: JP 05 202038 A (SUMITOMO) 10 August 1993 (1993-08-10)
- D7: DATABASE BEILSTEIN 28 November 1988 (1988-11-28), XP002322768
Database accession no. BRN: 677345

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/039775

D8: DATABASE BEILSTEIN 1988, XP002322769 Database accession no. BRN:
1008075

D9: DATABASE BEILSTEIN 1988, XP002322863 Database accession no. BRN:
1013052

D10: WO 02/46174 A (GLAXO) 13 June 2002 (2002-06-13)

Novelty (Article 33(2) PCT)

D1 to D9 disclose compounds which are encompassed by the present claim set. The present claim set is therefore not novel.

Inventive Step (Article 33(3) PCT)

D1 and D10 disclose PPAR modulators, D1 can be regarded as the closest prior art.

The problem of the application was the provision of new PPAR modulators.

Since the present compounds have already been disclosed in D1 the present invention lacks an inventive step.

Clarity (Article 6 PCT)

The claims contain many definitions and expression which are unclear within the meaning of Article 6 PCT, e.g. the terms "heteroalkyl", "heterocycloalkyl", the definition for an "aliphatic linker" (which could be according to the definition in claim 1 e.g. an oxygen atom) and the definition of R32 as a bond.